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Large numbers of Gulf War veterans have expressed concerns about their physical health. The current project sought to identify and examine the role of a number of potential predictors on two health outcomes – reported health symptoms and health functioning. Specifically, the extent to which female gender, psychiatric status (most notably PTSD), and perceived environmental exposure affect physical health were examined. Mailed questionnaires were sent to a previously assessed cohort of 2949 Gulf War veterans. A total of 1280 (1158 men, 122 women; 43.4% response rate) returned completed questionnaires. Attempts to assess and control for bias due to nonresponse are underway. Preliminary results show that although female veterans report more health symptoms than their male counterparts, few if any differences are found for physical health functioning. PTSD and increased levels of perceived environmental exposure, however, predict both an increase in reported health symptoms and decreased health functioning. Furthermore, effects for PTSD and environmental exposure do not appear to differ across gender. These results suggest that Gulf War veterans may be experiencing decrements in functional health, and these decrements are associated with psychological as well as environmental variables. Additional analyses exploring these and other relationships are ongoing.

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Introduction

With women's increasing proportional representation in the U.S. Armed Forces (Dienstfrey, 1988; Government Accounting Office, 1992; Wolfe, Mori, & Krygeris, 1994; Wolfe, Schnurr, Brown, & Furey, 1994; Wolfe, Brown, & Kelley, 1993), there is rapidly growing interest in factors directly related to female soldiers' total physical and psychological well-being. Of particular interest are variables that potentially influence positive readjustment during and immediately following war-time deployment. To gather unique data on this topic, this study expanded the fourth observation phase of an ongoing longitudinal project involving New England-area Gulf War Army veterans where the overall aim was the characterization of components of positive readjustment following war-time service. Correspondingly, the goal of this *new* proposed phase was to examine the role of potential predictors of functional health status, using current self-reported health status and health perceptions as health status indicators. Carefully defined measures of well-being (e.g., functional well-being/quality of life, physical health status, perceptions of health) served as the primary outcome variables of interest. A particular emphasis was the role of *female* gender as a possible predictor of functional health status and post-deployment health perceptions (Verbrugge, 1985). Other potential predictors of interest, derived from prior research emphasizing their importance (e.g., Wolfe, Schnurr, et al., 1994), included symptoms of post-traumatic stress disorder (PTSD) and self-reported exposure to potentially hazardous environmental agents.

The primary objective of this study was to identify and describe the effects of potential predictors on the functional health status and health perceptions of male and female veterans approximately five years after their deployment to the Gulf; and to examine if and how identified "risk" factors differed between female and male veterans. A secondary objective of the proposed project was to ascertain the prevalence of multiple chemical sensitivity (MCS)-like symptoms reported among this population.

The goals of the investigation were: (a) to identify and examine the role of potential predictors on two critical outcomes - current health status and individual health perceptions, and (b) to evaluate predictors' relevance for veterans' functional health status or disability. A primary emphasis was on investigating the role of gender, specifically, whether female gender was a significant factor in predicting either functional health status or health perceptions.

Research Design and Methodology

Study Design

In our original SOW, we stated that we intended to conduct face-to-face evaluations with approximately 200 women and 1000 men from the Ft. Devens cohort of US Army Gulf War veterans. But in fact, we felt the need to change the study design to that of a mail survey to the entire cohort. This change was initiated in an effort to obtain data on more participants that would represent a more accurate characterization of the entire cohort in a more feasible and economically efficient manner and to reduce subject burden (related to traveling time). We requested and received permission for the switch to a mail survey during discussions with Juanita Bourne in September and October 1996. Only the method of gathering information and the total eligible subject pool changed from the original SOW; the content areas and hypotheses remained unchanged. We described this design change in our first Annual Report (submitted 10/10/96) after conversations with Juanita Bourne and the change was approved by the local VA IRB, approved by DA in writing on 7/9/97, and referred to in all subsequent project updates. (A documented chronology of these events is attached in Appendix A.)

Therefore, the study protocol involved administering a mailed survey to the entire U.S. Army Ft. Devens cohort (n=2949). The main survey components included: (1) assessment of functional status (e.g., SF36 (Ware 1993; Ware 1994), review of medical history and current health status, (2) comprehensive assessment of psychological and physical health symptoms, (3) comprehensive assessment of self-reported environmental exposure history, (4) a review of military and nonmilitary high magnitude life stressors, (5) assessment of social support, (6)

psychological symptomatology (e.g., PTSD, depression) and (7) assessment of standard demographic information (e.g., work, military, educational histories).

Survey Procedures

All original cohort members from the Ft. Devens Reunion Survey cohort (n=2949) were eligible for this project and were targeted aggressively for participation, via four mailing waves starting in March 1997 (see Figure 1 for a flowchart overviewing the subject recruitment process at each of the waves of mailing). Because the Ft. Devens cohort has been longitudinally followed, addresses from previous waves of data collection were available for all but 17 persons. Nonetheless, members of the cohort were quite mobile, with many of them changing residences annually. Questionnaires returned with an updated or forwarding address were resent. For those returned undeliverable, current addresses were sought using various telephone and Internet locator services. A small token (a key chain with the study's logo) was offered as an incentive for returning a completed questionnaire. After four weeks, a reminder postcard was mailed to those who had not returned a completed questionnaire. After an additional two weeks, the questionnaire was resent to all non-respondents, with another reminder postcard two weeks later. A third mailing of the survey to those non-respondents was made after another 12 weeks.

After three complete mailings, a total of 1290 participants (44% of the cohort; a rate very comparable to other large-scale military and veteran surveys 6 to 8 years after the initial wave of data collection) had returned completed questionnaires as of March 1998. At this point, all those who had not returned a completed questionnaire were considered non-responders. To attempt to assess any potential non-response bias, we compared all responders (N=1290) and non-responders (N=1659) on a number of characteristics from the first wave of data collection in 1991. In terms of demographics, we found a number of statistically significant differences. Non-responders were less likely to be female (7%) than were responders (9%), non-responders were less likely to be married (53%) than were responders (62%), non-responders were younger

(28.7 years) than responders (32.0 years), non-responders were less educated (13.0 years) than responders (13.3 years), non-responders were more likely an ethnic minority (22%) than responders (11%). The only military variable on which responders and non-responders differed was military status (active duty versus Reserves or National Guard), with non-responders more likely to come from active duty (32%) than responders (23%). Although no physical health variables were included in the original survey, a number of psychological variables were included and there were no differences on psychological or stress variables, including posttraumatic stress symptoms and reported combat exposure. Thus, although there were some differences between responders and non-responders on demographic characteristics, there were no differences on any psychological outcome variables. The young, active duty, minority participants were the most underrepresented in the Time 4 data collection.

Given that there did appear to be differences between responders and non-responders, measures were taken to address this and hopefully control for any potential non-response bias. The first and most straightforward technique was to control for these demographic differences in all analyses. For instance, in the regressions used to test hypotheses 2 and 3, all of these demographic and military variables were included as covariates.

A second, and much more complex, technique for controlling for any potential non-response bias was to assess data on a small subset of non-responders and use this data to develop a weight variable that would statistically correct for any non-response bias. Although not proposed in the original grant, we believed this technique was warranted and would increase the likelihood of scientific publication of these results. We targeted a randomly selected subcohort of 120 of these non-responders for aggressive follow-up. An outside research firm with extensive experience collecting data from veterans of the U.S. Armed Forces was recruited to help in locating, contacting, and administering the surveys. Numerous aggressive procedures were employed to locate these non-responders, including searches of telephone directory databases, credit history reports, and a federal interagency agreement permitting a search for

updated addresses using IRS databases. In addition, a permanent address of a family member, collected as part of the initial questionnaire in 1991, was also pursued. The social security death index was consulted to establish if any of these non-responders were deceased.

Even with these extensive procedures, 42 of the targeted non-responders (representing 35% of the targeted non-responders) could not be located. Of the 78 that were located, however, 62 (79.5%) were contacted and agreed to complete the questionnaire. Thus, although many of the targeted non-responders could not be located, a large majority of those located provided data. However, because only approximately half of those identified for follow-up participated, for the current report we have employed the first technique (including a number of demographic and military variables as covariates) to attempt to minimize the effects of non-response bias on our results. The utility of the use of statistical weighting is being pursued for possible inclusion in future manuscript submissions.

Power and Sample Size Considerations

Fewer females did participate in the study (n=122) than was assumed when calculating the original power goals (n=200). However, this difference does not significantly alter the study's ability to detect gender differences from what was originally proposed, where the SF-36 subscales scores and a categorical measure of increased health symptoms (CDC case definition of Gulf War illness) are the outcomes of interest. As was stated in our original proposal, at least a 5-10 point significant difference would be detectable between men and women on the various subscales of the SF-36. Also, given estimated PTSD symptom prevalences of 15% in women and 7% in males in our cohort, it would be possible to detect 20 point differences on various SF-36 subscales between females with PTSD and without PTSD symptomatology. Assuming that "high" exposure to oil smoke occurred in 30% of participants, we would be able to detect a 15 point difference on various subscales between females with and without reported environmental exposure. Finally, it would be possible to detect a 5-10 point difference between the female group means for our study sample compared to established

norms for various SF-36 subscales. For the Physical Component and Mental Component Summary scores (Ware, 1994) of the SF-36, with a sample size of 122 females, it would be possible to detect a 2-5 point gender difference. Table 1 reports the specific sample size requirements to detect differences on selected SF-36 subscales based on work by Ware (1993).

Analyses

Hypothesis 1. The first hypothesis was that women veterans, as compared to male veterans, would report higher levels of health symptoms and lower levels of health functioning. Health symptoms were measured using a comprehensive, 52-item checklist of common health symptoms such as headaches, backaches, fatigue, difficulty concentrating, etc. Recent research on Gulf War illness has attempted to evolve a case definition for the most common set of symptoms expressed by ill GW veterans (Fukuda et al., 1998). Building on these efforts, we undertook to replicate the case definition described by Fukuda et al. (1998) using the same factor structure (i.e., fatigue, mood & cognition, musculoskeletal). Given the substantial overlap of our symptom questions with those of Fukuda et al. (1998), we reasoned that the ability to replicate those investigators' case definition in a different sample would help substantiate the existence of a multi-faceted health syndrome in male and female veterans. Further, classifying symptoms in this fashion could represent a more parsimonious method for examining salient predictors and specific health outcomes in our cohort.

To construct the case definition, we used the Centers for Disease Control and Prevention (CDC) multisystem criteria for Gulf War illness in which a case was defined as having 1 or more symptoms from at least 2 of 3 designated categories (fatigue, mood-cognition, and musculoskeletal). Cases were further broken down into "mild" and "severe." A mild case was indicated when at least one of the criteria-defining symptoms was indicated as occurring only "somewhat." In contrast, a severe case was indicated when all criteria-defining symptoms were indicated as occurring "a lot." Differences between men and women are reported for both mild and severe cases.

The SF-36 (Ware 1993; Ware 1994), a well-known, nationally validated measure of both physical and mental health functioning, was used to evaluate the health functioning of our cohort of Gulf War veterans. The SF-36 is comprised of 8 subscales, four of which measure aspects of physical health functioning (physical functioning, role-physical, bodily pain, general health) and four of which measure aspects of mental health functioning (social functioning, role-emotional, vitality, mental health). In addition, 2 overall indices of physical functioning and mental functioning were created by differentially summing across the 8 subscales. Differences between men and women are reported for both the 8 individual subscales as well as the 2 indices of health functioning.

Hypothesis 2. The second hypothesis was that PTSD symptomatology and reported hazardous environmental exposure would constitute risk factors that predict poorer functional status and more self-reported health symptoms following Gulf deployment in this cohort. This hypothesis was tested by regressing the measures of a health symptom-based case definition of Gulf War illness and the physical and mental component scores of the SF-36 described above on a number of demographic, psychological, and environmental exposure variables. Specifically, the demographic variables included gender, age, education, marital status, ethnicity, military status, military rank, and current military status. Combat exposure was measured immediately upon return from the Gulf using a 34-item scale designed to assess a number of stressors unique to the Gulf War. PTSD was measured using the PTSD Checklist. This scale is comprised of 17 items that directly pertain to the 17 DSM-IV symptoms of posttraumatic stress disorder and allows for a presumptive diagnosis of PTSD. Based on both previous research with Gulf War veterans and anecdotal descriptions, a large number of self-reported environmental exposures were assessed. These included smelling oil smoke, diesel, insecticides, and chemicals, having a heater where they slept, having a cold or flu in the Gulf, going to the clinic in the Gulf, receiving any medical treatment while in the Gulf, consuming

antibiotics while in the Gulf, having an anthrax shot, consuming anti-nerve gas pills, and being on formal alert for chemical attack.

Hypothesis 3. The third hypothesis was that there would be a differential effect of gender in conjunction with both PTSD and reported environmental exposures on health symptoms and functional well-being. This hypothesis was tested by a series of regressions identical to those used to test hypothesis 2 except for the addition of gender interactions with PTSD and environmental exposures.

Multiple chemical sensitivity. Although it was not a primary hypothesis of this study, one objective of this study was to investigate the prevalence of multiple chemical sensitivity (MCS)-like symptomatology in this cohort, as anecdotal reports have indicated elevated levels of sensitivity to common odors and smells in Gulf War veterans.

One of the first steps in ascertaining the prevalence of MCS-like symptoms among our study population was to develop a survey instrument to identify subjects with such symptoms. At the time we initiated this study, there was only one survey instrument that had been validated to assess MCS symptoms (Kipen et al., 1995). However, due to the length of that scale, we conducted a small case-control study of MCS patients (meeting Cullen's definition of MCS; Cullen, 1987) and non-ill age- and sex-matched control subjects in order to identify a parsimonious set of questions, from the 122-item Kipen scale, that had high sensitivity and specificity for screening for individuals with Multiple Chemical Sensitivity Syndrome. A stepwise selection procedure for two-group discriminant analysis revealed that the main contributors to the discrimination of the cases and controls were self-reported reactions to copy machine emissions, marking pens, aftershave, window cleaner, nylon fabric, pine-scented products, and rayon material. If a positive response to these factors was used as the sole method for discriminating cases from controls only one of the 41 cases was misclassified as a control while none of the controls was misclassified as a case. A manuscript describing this study, the data

analyses, and a presentation of our seven item 'short-list' of discriminatory odors and smells has been prepared and is currently under review for publication (Hu et al., 1999).

These seven 'discriminatory' items were included in a list with 11 other common odors and smells in the mail survey administered as part of this study in order to screen for MCS-like symptoms in this Gulf War veteran population. The prevalence of these MCS-like symptoms and a test for a differential effect of gender are reported.

Longitudinal results. One of the major strengths of the Ft. Devens cohort is the multiple waves of data that have been collected over the past 8 years. Although not comprehensive, both the rates and stabilities of PTSD are reported. As with all previous analyses, differences across gender are reported.

Results

Table 2 presents a number of demographic characteristics of participants separately for men and women, with a statistical test for any differences between the men and women. As is seen in the table, our sample is predominantly white, enlisted personnel, and members of the Reserve and National Guard. Compared with the men, women in our sample are younger, better educated, more likely to be single and a member of a minority race, and less likely to be employed. Although men and women are statistically different on a number of characteristics, the magnitude of the differences is fairly small.

Hypothesis 1

Our first hypothesis was that female veterans, compared to male veterans, would report more health symptoms and lower levels of functional well-being. Table 3 presents health symptom data separately for men and women, including a test for gender differences. Supporting our hypothesis, based on a 52-item health symptom checklist, female veterans endorse significantly more health symptoms than do male veterans. On average, female participants indicated they had experienced 17 of the 52 health symptoms over the past 4 weeks. Male veterans indicated they had experienced almost 14 symptoms over the past 4

weeks. As is seen in Table 3, the primary symptoms being endorsed by our participants are quite diverse, including both somatic complaints (e.g., backaches, neckaches, joint pains) as well as more psychosomatic complaints (e.g., forgetfulness, unsatisfying sleep, anger or irritability, etc.). No easily discernible pattern is indicated when gender differences are examined at the individual symptom level, with women endorsing almost all symptoms at a higher rate than are men (a pattern common in non-veteran samples as well).

Using a subset of these 52 symptoms, a case definition of Gulf War illness based on work by the CDC (Fukuda et al., 1998) was defined. As seen in the bottom of Table 3, approximately 60% of our cohort met criteria for Gulf War illness, approximately evenly split between "mild" and "severe" cases. When rates are compared between men and women, we see that although there are no differences between men and women for "mild" caseness, there are differences for "severe" cases, with women more likely to meet criteria for "severe" caseness than men.

The second half of hypothesis 1, that the women would show lower levels of health functioning than the men, was less well supported. In our cohort, women were lower than men on mental health functioning (both on the overall mental health score and 3 of the 4 mental health subscales; see Table 4), but there were no significant differences between women and men on physical health functioning.

A related question of interest is the health of the Gulf War veterans relative to the general population. One strength of the SF-36 as a measure of health functioning is the extensive work that has been done to establish population norms. Compared to a representative U.S. sample of women aged 35-44 years, the women in our cohort scored on average at about the 25th percentile for both overall physical health functioning and overall mental health functioning. Likewise, the men scored near the 25th percentile of a representative U.S. sample of men aged 35-44 years on both physical and mental health functioning. Thus, compared to the general U.S. population, our Gulf-deployed veterans may be experiencing some deficits in

health functioning. These findings may prove to be notable given the expected 'robustness' of a deployed cohort.

Hypothesis 2

Our second hypothesis was that PTSD symptomatology and reported hazardous environmental exposure constitute risk factors that predict poorer functional status and more self-reported health symptoms following Gulf deployment in this cohort. We tested this hypothesis with a number of regression models. We first regressed Gulf War illness on PTSD and an index of environmental exposures, controlling for a number of background and demographic variables including gender, age, race, education level, employment status, marital status, military status, military rank, and reported combat exposure (assessed immediately upon return from the Gulf at Time 1). Given that Gulf War illness is defined categorically (noncase, case-mild, and case-severe), this was a polytomous logistic regression. We replicated this regression for functional health status in two regressions, one for physical health functioning and one for mental health functioning. These analyses build directly on our work in prior phases (e.g., Wolfe, Erickson, Sharkansky, King, & King, in press).

Before presenting these results, we first overview the rates of PTSD and reported environmental exposures in the cohort. Table 5 shows the rates of PTSD, combat exposure (collected immediately upon return at Time 1), and reported environmental exposures for both men and women. Rates of PTSD (based on the PTSD Checklist) were fairly high at 20% for women and 15% for men. The higher rate for women, although not statistically significant in this instance, is consistent with previous waves of this cohort (e.g., Wolfe, Erickson et al., in press) as well as numerous other studies documenting that women are at higher risk for PTSD than men. These rates also represent a small increase over previous study waves, which showed rates of PTSD between 8 and 18% for men and women, respectively, and suggest slight but notable increases in PTSD rates over time. Further details on related longitudinal analyses for men and women are presented below.

Although there were no differences seen between men and women on combat exposure, there were differences on a number of reported environmental exposures. Women reported being more likely to smell insecticide in the air, have a heater in their sleeping area, be seen in a clinic while in the Gulf, receive medical treatment while in the Gulf, and be placed numerous times on formal alert for chemical attack.

The rightmost column of Table 6 reports the odds ratios associated with each of the predictors in the polytomous logistic regression predicting Gulf War illness. Controlling for significant effects of employment status, general psychological distress (measured by the Global Severity Index of the Brief Symptom Inventory) and four environmental exposures were significantly associated with Gulf War illness caseness. Those veterans reporting exposure to oil smoke were approximately 1.5 times more likely to meet criteria for Gulf War illness than those not reporting exposure to oil smoke. Similarly, those reporting smelling chemicals and those reporting consuming between 1 and 21 anti-nerve gas pills were also approximately 1.5 times more likely to meet criteria than those without these exposures. Furthermore, those reporting having consumed 22 or more anti-nerve gas pills were over twice as likely to meet criteria for Gulf War illness.

A fairly different pattern was seen when we regressed physical health functioning on our predictors and covariates. As seen in the left column of Table 6, being unemployed and scoring high on general psychological distress were also associated with poor functioning. However, a number of additional demographic covariates were significantly associated with poor physical functioning, including older age, being married, and being an enlisted personnel (as opposed to an officer). Controlling for these variables, three environmental exposures were associated with physical functioning. Those reporting exposure to diesel smells, those who received medical treatment while in the Gulf, and those who consumed 22 or more anti-nerve gas pills had significantly poorer physical health functioning. This model accounted for 30% of the variance in physical health functioning.

Finally, the middle column of Table 6 reports results from regressing mental health functioning on these covariates and predictors. Controlling for significant effects for age, ethnicity, and civilian status, general psychological distress, being seen in a clinic while in the Gulf, receiving antibiotics in the Gulf, and consuming 22 or more anti-nerve gas pills were associated with mental health functioning. The model accounted for almost 60% of the variance in mental health functioning.

Findings from these 3 regressions, particularly those two predicting Gulf War illness and physical health functioning, provide mixed support for our second hypothesis. Although general psychological distress was predictive of both Gulf War illness and physical health functioning, PTSD based on the PTSD Checklist was not. This may be due in part to the overlap between general psychological distress and PTSD, particularly in this cohort where the rate of PTSD is not extremely high. Thus, although PTSD per se is not associated with decreased physical health, there is support for a psychological component. In addition, the pattern with reported environmental exposures is complex, with only the consumption of large quantities of anti-nerve gas pills consistently predictive of all three outcomes. Otherwise, a number of different exposures were associated with only one of the three outcomes.

Hypothesis 3

Our third hypothesis was that there would be a differential effect of gender in conjunction with PTSD symptomatology and reported environmental exposure on health status and functional well-being. We tested this hypothesis by replicating the previous 3 regressions, adding the interactions between gender and PTSD and gender and reported environmental exposures as additional predictors. A significant gender by PTSD interaction would suggest that the effects of PTSD on health outcome differ for men and women. Similarly, a significant gender by environmental exposures interaction would suggest the effects of environmental exposures on health outcome differ for men and women.

This hypothesis of a differential effect had mixed support (see Table 7 for the full results of the 3 regressions). Across all three outcomes, there was no evidence for a differential effect of PTSD across men and women. It is worth noting, however, that although the effect for Gulf War illness is not significant, it was fairly substantial in magnitude. Women with PTSD were over 5 times more likely to meet criteria for Gulf War illness. The failure of this effect to reach statistical significance may be related to the combination of relatively few women in the cohort (about 120) and the fairly low rates of presumptive PTSD (around 20% for women). Predicting Gulf War illness, three of the reported environmental exposures interacted with gender; two showing a stronger effect for women and one showing a stronger effect for the men. The smell of insecticide and smelling chemicals interacted with gender such that the effect was stronger for women than men. In contrast, the smell of oil was a more highly predictive of Gulf War illness for the men.

For physical health functioning, all of the interactions between gender and reported environmental exposures were nonsignificant. For mental health functioning, the gender by medical treatment interaction was significant, with the relationship between medical treatment and mental health functioning stronger for women than for men.

MCS Symptoms

Table 8 presents the rates at which the men and women in our cohort endorsed the 18 common odors or smells associated with MCS-like symptoms. As expected, based on the literature, women endorsed individual exposures at higher rates than men. Over 15% of participants reported a sensitivity to at least one of the seven 'discriminatory' exposures that have been shown to discriminate those with MCS from those without. Furthermore, women endorsed a sensitivity to at least one of the seven 'discriminatory' exposures at a substantially higher rate than men (22% vs. 15%, respectively). These data suggest that our Gulf War veterans are experiencing a certain level of MCS-like symptoms and this may be a topic worthy of future study.

Longitudinal Rates of PTSD

One of the advantages of collecting data longitudinally for a cohort is the opportunity to track and predict both the changes and stabilities of certain outcomes over time. The entire Ft. Devens cohort of Gulf War veterans has now been assessed on three occasions, allowing us to examine how certain outcomes are changing over the 8 years since the Gulf War. An excellent example of this is the change in the rate of PTSD over the 3 measurement occasions since the Gulf War. Using only participants who provided complete data at all 3 waves, approximately 8% of the women and 3% of the men met criteria for presumptive PTSD based on the Mississippi Scale at Time 1. Approximately 2 years later, the rate of PTSD had increased to approximately 16% among the women and 8% among the men. In the current wave, approximately 4 years after the second wave, the rates of PTSD are now 20% for the women and 15% for the men. Thus, it appears that the rates of PTSD in the Ft. Devens cohort are both consistently higher among women and have consistently increased since the Gulf War.

In addition to looking at the rates over time, we can also examine the stability or autoregressive effect of meeting criteria for PTSD. For example, those who met criteria for PTSD at Time 1 were approximately 15 times more likely to meet criteria for PTSD at Time 2 than were those who did not meet criteria at Time 1. This stability coefficient was roughly the same from Time 2 to Time 4, and these did not differ for men and women. These data suggest that meeting criteria for presumptive PTSD represents a significant risk factor for PTSD at a later time. A manuscript expanding these analyses and including a number of additional predictors using just the Time 1 and 2 data is due to be published soon (Wolfe, Erickson, et al., in press), and additional analyses incorporating all 3 waves into a comprehensive model of the course and predictors of PTSD over an 8-year period are planned.

Conclusions

A number of important patterns emerge from these data. First, these data suggest that there are appreciable levels of physical health concerns among Gulf War veterans. In terms of

functional status for physical health, for example, participants scored on average at the 25th percentile based on age and gender matched national normative data. Functional status data confirm that, at least for our cohort, Gulf War veterans' concerns exceed subjective health complaints. In addition to this functional measure, we also categorized participants on a Gulf War illness variable using the newly constructed CDC case definition for these problems. Once again, we found significant health decrements, with over half of participants meeting the case definition at a mild or severe level. Our rate of illness is somewhat higher than that found by other researchers. One possible explanation is that our case definition lacks a duration parameter. Still, close to 30% of our participants met criteria at the severe case level, suggesting that notable levels of illness exist.

Second, female Gulf War veterans, although reporting more health symptoms than their male counterparts, do not appear to differ in terms of physical health functioning. Women overall reliably reported more individual health symptoms than men. This was also reflected in a higher percentage of women meeting the case definition for severe Gulf War illness. Our findings on illness and symptoms in women are consistent with data in a number of other samples. One possible explanation is that the reported health symptoms include a certain proportion of psychosomatic variables that differ between men and women. This explanation is consistent with our finding that women had lower mental health functioning compared to men. Our findings for women are also in broad agreement with a number of national epidemiological studies of psychiatric syndromes in men and women as well as age-matched gender norms for the SF-36. Hence, the difference between men and women in our sample is comparable to those found in relevant comparison groups.

Third, physical health outcomes appear to be related to both general psychological distress and reported environmental exposure. This finding was confirmed by analyses using a case definition for Gulf War illness. There are few significant differences in this relationship between men and women with the exception of the following. For the environmental exposures,

gender moderated the relationship between oil exposure, chemical smells, and insecticides. Consistent with our predictions, the relationships between chemicals and insecticides and Gulf War illness were stronger for women than men. In contrast, the effects for oil smoke were stronger for men than women. These results suggest that there may be a gender based differential susceptibility to environmental exposures. However, it is possible that our ability to detect gender differences was limited by the number of women in our total cohort from the outset. Further studies examining the interaction of gender and environmental exposures are warranted.

An interesting aspect of the longitudinal analyses available with this cohort is the observation that rates of PTSD increase over time. This effect does not appear to differ for men and women as the proportional difference in gender based rates is stable over several time periods. Although health data immediately following the war are not available for this cohort, it may prove worthwhile to continue to track physical health status over time to determine if a similar trend emerges in this domain.

Finally, the observed prevalence of MCS-like symptoms among participants (~15-20%) is similar to that observed in other Gulf War veteran populations even though methods of assessment are somewhat different.

In summary, these findings are provocative and indicate that Gulf War veterans suffer from a number of problems. Continued monitoring is needed to make more definitive statements about the etiology of these health problems.

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Table 1

Sample Size Requirements to Detect Differences on Selected SF-36 Subscales

	Number of points difference		
Scale	5	10	20
Physical Functioning Subscale	342	86	22
General Health Subscale	262	66	17
Mental Health Subscale	207	52	14

Note. Data taken from Ware (1993). α=0.05, two-tailed t-test, power=80%.

Table 2

Demographics of Responders by Gender

Variable	Women (N=126)	Men (N=1218)	Test of Gender Difference
Mean (SD) age in years	35.2 (7.4)	38.1 (9.0)	$t(163.5)= 4.1$, $p<.01$
Mean (SD) education in years	13.8 (2.0)	13.3 (1.9)	$t(1280)= -2.9$, $p<.01$
% White	85	91	$\chi^2(1)=4.8$, $p<.05$
% Currently employed	86	93	$\chi^2(1)=8.8$, $p<.01$
% Currently married	43	70	$\chi^2(1)=37.1$, $p<.01$
% Enlisted when deployed to Gulf	90	92	$\chi^2(1)=0.3$, $p=.57$
% Reserve/National Guard when deployed to Gulf	78	77	$\chi^2(1)=0.1$, $p=.75$

Table 3

Reported Health Symptoms and Gulf War Illness by Gender

Variable	Women	Men	Test of Gender Difference
Health Symptom Checklist (52 symptoms)			
Mean (SD) health symptoms endorsed	17.0 (12.7)	13.8 (11.4)	$t(1340)= -2.9$, $p<.01$
Most prevalent symptoms (% endorsed)			
Joint pains	52	56	$\chi^2(1)=0.8$, $p=.37$
Forgetfulness	65	54	$\chi^2(1)=4.9$, $p<.05$
Fatigue	67	53	$\chi^2(1)=8.9$, $p<.01$
Restless or unsatisfying sleep	54	52	$\chi^2(1)=0.3$, $p=.60$
Muscle weakness or fatigue	53	47	$\chi^2(1)=1.9$, $p=.17$
Backaches	54	46	$\chi^2(1)=3.1$, $p=.08$
Excessive anger or irritability	51	45	$\chi^2(1)=1.6$, $p=.20$
Headaches	56	40	$\chi^2(1)=11.3$, $p<.01$
Neckaches or stiffness	44	40	$\chi^2(1)=1.2$, $p=.28$
Gulf War Illness Case Definition			
Noncase	37	42	Reference category
Case – Mild	24	29	$\chi^2(1)=0.1$, $p=.78$
Case – Severe	39	29	$\chi^2(1)=4.3$, $p<.05$

Table 4

Reported Health Functioning (based on the SF-36) of Gulf War Veterans Reported Separately by Gender

Variable	Women	Men	Test of Gender Difference
Physical Component Score (Mean[SD])	46.2 (11.8)	47.4 (10.1)	t(140.8)=1.0, p=.30
Physical Functioning	80.6 (23.1)	84.1 (21.4)	t(1342)=1.7, p=.08
Role Physical	65.6 (39.6)	72.3 (37.2)	t(1337)=1.9, p=.06
Bodily Pain	64.7 (27.9)	67.0 (25.2)	t(1340)=1.0, p=.33
General Health	54.5 (25.0)	57.4 (24.5)	t(1339)=1.3, p=.21
Mental Component Score (Mean[SD])	42.6 (13.7)	45.4 (11.9)	t(141.4)=2.1, p<.05
Vitality	44.0 (24.3)	48.6 (23.7)	t(1341)=2.1, p<.05
Social Functioning	69.9 (28.3)	77.1 (26.0)	t(1342)=2.9, p<.01
Role Emotional	63.7 (43.6)	72.5 (39.0)	t(1331)=2.4, p<.05
Mental Health	63.5 (21.5)	66.9 (20.9)	t(1340)=1.7, p=.09

Table 5

PTSD, Combat Exposure, and Environmental Exposures of Gulf War veterans by Gender

Variable	Women	Men	Test of Gender Difference
% PTSD	20	15	$\chi^2(1)=2.1$, $p=.14$
Combat Exposure at Time 1 (Mean[SD])	6.7 (4.2)	7.0 (4.8)	$t(161.6)=0.7$, $p=.47$
Reported Environmental Exposures (%)			
Oil Smell in Air	58	63	$\chi^2(1)=1.0$, $p=.31$
Insecticide Smell in Air	36	27	$\chi^2(1)=4.1$, $p<.05$
Diesel Smell in Air	59	65	$\chi^2(1)=1.8$, $p=.18$
Chemical Smell in Air	12	14	$\chi^2(1)=0.3$, $p=.58$
Had a heater where slept	73	60	$\chi^2(1)=7.8$, $p<.01$
Seen in Clinic While in Gulf	55	36	$\chi^2(1)=17.8$, $p<.01$
Had Cold or Flu in Gulf	48	42	$\chi^2(1)=2.0$, $p=.16$
Received medical treatment in Gulf	63	51	$\chi^2(1)=7.1$, $p<.01$
Had an anthrax shot in Gulf	57	66	$\chi^2(1)=3.5$, $p=.06$
Received Antibiotics While in Gulf	34	31	$\chi^2(1)=0.5$, $p=.50$
Consumed 22+ Anti-Nerve Gas Pills	19	17	$\chi^2(1)=0.4$, $p=.54$
Placed on Formal Alert for Chemical Attack 11 or more times	52	39	$\chi^2(1)=8.0$, $p<.01$

Table 6

Physical Functioning, Mental Functioning, and Gulf War Illness Caseness Regressed on Demographic, Psychological, and Environmental Exposures

Predictor	Physical Component Scale $R^2 = 0.30$	Mental Component Scale $R^2 = 0.57$	Gulf War Illness Caseness c = 0.85
Female gender	-0.12	-0.20	1.00
Age	-.19*	0.10*	1.01
Caucasian	-0.23	-2.10*	1.65
Employed	5.55*	-1.11	0.48*
Married	-1.41*	0.84	1.25
Enlisted personnel	-2.95*	1.12	1.01
Reserve status (when deployed)	-0.27	-0.26	1.09
Civilian	0.01	1.04*	0.77
Reported combat exposure (Time 1)	-0.01	0.01	1.00
PTSD at Time 4	-1.08	0.59	0.81
General psychological distress	-4.95*	-14.70*	19.75*
Oil smell in air	-0.38	-0.29	1.49*
Diesel smell in air	-1.43*	0.46	1.15
Insecticide smell in air	-1.08	0.28	1.05
Chemical smell in air	-1.06	0.07	1.69*
Had a heater where slept	0.49	0.24	1.22
Had cold or flu in Gulf	-0.34	-0.61	1.00
Seen in clinic while in Gulf	-0.43	-2.10*	1.14
Received medical treatment in Gulf	-1.42*	0.92	1.12
Received antibiotics while in Gulf	-0.56	1.79*	1.28
Had anthrax shot in Gulf	0.27	0.89	1.21
Consumed 1-21 Anti-Nerve Gas Pills	-0.24	-0.87	1.46*
Consumed 22+ Anti-Nerve Gas Pills	-1.81*	-1.72*	2.19*
Placed on Formal Alert for Chemical Attack 3-10 times	-0.10	0.39	0.82
Placed on Formal Alert for Chemical Attack 11 or more times	-1.23	0.14	1.05

Note. c=rank correlation index of predictive ability of the model. *p<.05

Table 7

Physical Functioning, Mental Functioning, and Gulf War Illness Caseness Regressed on Demographic, Psychological, Environmental Exposures, and Gender Interactions

Predictor	Physical Component Scale $R^2 = 0.32$	Mental Component Scale $R^2 = 0.59$	Gulf War Illness Caseness c = 0.85
Female gender	-0.73	0.01	1.49
Age	-0.19*	0.10*	1.01
Caucasian	-0.05	-2.23*	1.71*
Employed	5.58*	-1.17	0.46*
Married	-1.51*	0.95	1.27
Enlisted personnel	-3.16*	1.11	1.11
Reserve status (when deployed)	-0.16	-0.29	1.08
Civilian currently	-0.09	1.10*	0.76*
Reported combat exposure (Time 1)	-0.01	0.01	1.00
PTSD at Time 4	-1.01	0.57	0.78
General psychological distress	-4.96*	-14.72*	21.27*
Oil smell in air	-0.31	-0.32	1.44*
Diesel smell in air	-1.34*	0.51	1.08
Insecticide smell in air	-1.13	0.35	1.14
Chemical smell in air	-1.13	0.00	2.10*
Had a heater where slept	0.52	0.21	1.15
Had cold or flu in Gulf	-0.28	-0.64	1.00
Seen in clinic while in Gulf	-0.30	-2.45*	1.09
Received medical treatment in Gulf	-1.61*	1.26	1.13
Received antibiotics while in Gulf	-0.51	1.75*	1.30
Had anthrax shot in Gulf	0.39	0.87	1.17
Consumed 1-21 Anti-Nerve Gas Pills	-0.37	-0.80	1.43*
Consumed 22+ Anti-Nerve Gas Pills	-2.07*	-1.55	2.34*
Placed on Formal Alert for Chemical Attack 3-10 times	0.02	0.29	0.76
Placed on Formal Alert for Chemical Attack 11 or more times	-1.22	0.12	1.04

Table 7 (continued)

Predictor	Physical Component Scale $R^2 = 0.32$	Mental Component Scale $R^2 = 0.59$	Gulf War Illness Caseness c = 0.85
Gender by PTSD interaction	0.24	1.15	5.63
Gender by oil smell interaction	3.94	-0.87	0.15*
Gender by diesel smell interaction	-2.68	2.20	1.29
Gender by insecticide smell interaction	-4.06	2.78	4.83*
Gender by chemical smell interaction	-3.24	-3.45	23.54*
Gender by heater interaction	2.12	-0.47	0.41
Gender by cold or flu interaction	-1.40	-3.00	1.20
Gender by clinic while interaction	4.55	-5.79	0.98
Gender by medical treatment interaction	-3.30	6.41*	0.83
Gender by antibiotics interaction	1.70	-0.73	0.66
Gender by anthrax shot interaction	-0.40	-1.02	0.91
Gender by Anti-Nerve Gas Pills (1-21) interaction	0.91	0.85	0.87
Gender by Anti-Nerve Gas Pills (22+) interaction	3.28	2.35	0.90
Gender by Formal Alert for Chemical Attack (3-10) interaction	0.19	-0.62	0.46
Gender by Formal Alert for Chemical Attack (11+) interaction	-0.98	-0.07	0.37

Note. c=rank correlation index of predictive ability of the model. *p<.05

Table 8

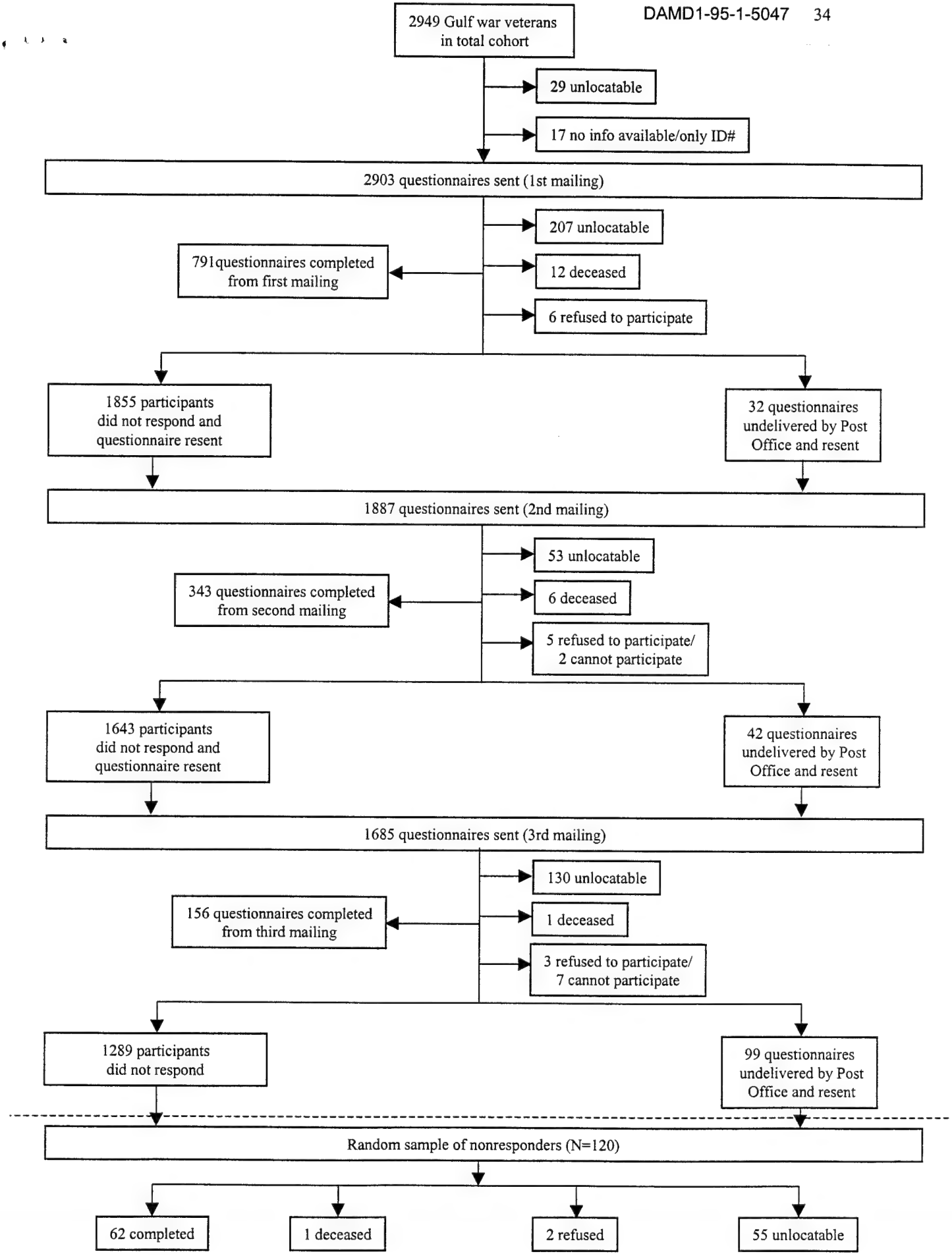
MCS-like Symptom-Causing Exposures Reported by Men and Women

Variable	Women	Men	Test of Gender Difference
Individual exposures (% endorsed)			
Perfume / Cologne	36	13	$\chi^2(1)=39.2$, $p<.01$
Air freshener	21	7	$\chi^2(1)=26.1$, $p<.01$
Public restroom deodorizer	16	5	$\chi^2(1)=18.6$, $p<.01$
New rugs	11	5	$\chi^2(1)=6.4$, $p<.05$
Pine scented products[a]	10	5	$\chi^2(1)=5.4$, $p<.05$
Window cleaner[a]	9	5	$\chi^2(1)=3.0$, $p=.09$
Furniture polish	7	4	$\chi^2(1)=2.7$, $p=.10$
Aftershave[a]	6	8	$\chi^2(1)=0.8$, $p=.38$
Dry cleaning	6	3	$\chi^2(1)=1.3$, $p=.26$
Newsprint	5	2	$\chi^2(1)=3.7$, $p=.06$
Pens[a]	3	5	$\chi^2(1)=0.4$, $p=.56$
Copy machines[a]	2	2	$\chi^2(1)=0.2$, $p=.63$
Nylon fabric[a]	2	1	$\chi^2(1)=1.7$, $p=.19$
Rayon material[a]	2	0	$\chi^2(1)=3.0$, $p=.09$
Cotton rugs	2	0	$\chi^2(1)=2.9$, $p=.09$
Inks	2	2	$\chi^2(1)=0.0$, $p=.98$
Magazines	2	1	$\chi^2(1)=0.4$, $p=.53$
Vinyl	0	1	$\chi^2(1)=1.11$, $p=.29$

Note. Those exposures marked with a superscript 'a' are the 7 substances found to maximally discriminate those with Multiple Chemical Sensitivity from those without.

Figure Caption

Figure 1. Flowchart of mailing procedure.


2949 Gulf war veterans in total cohort
29 unlocatable
17 no info available/only ID#
2903 questionnaires sent (1st mailing)
207 unlocatable
791questionnaires completed from first mailing
12 deceased
6 refused to participate
1855 participants did not respond and questionnaire resent
32 questionnaires undelivered by Post Office and resent
1887 questionnaires sent (2nd mailing)
53 unlocatable
343 questionnaires completed from second mailing
6 deceased
5 refused to participate/ 2 cannot participate
1643 participants did not respond and questionnaire resent
42 questionnaires undelivered by Post Office and resent
1685 questionnaires sent (3rd mailing)
130 unlocatable
156 questionnaires completed from third mailing
1 deceased
3 refused to participate/ 7 cannot participate
1289 participants did not respond
99 questionnaires undelivered by Post Office and resent
Random sample of nonresponders (N=120)
62 completed
1 deceased
2 refused
55 unlocatable

Appendix

Project Revision Chronology

1. 3/21/96 Submitted VA Research Progress Report indicating probable need to Project Revision Chronology switch to mailed survey format for whole cohort

2. 7/30/96 Letter received from DA indicating Annual Report for 9/11/95-9/10/96 due 10/10/96 (Pawlus).

3. 9/18/96 Additional investigator meetings of team planning to forego field interviews and switching to mailed survey of entire cohort, based on need for larger sample and avoidance of subject burden.

4. 10/96 Spoke with Juanita Bourne at DA re. proposed change to mail methodology; received verbal approval (A. Stern, Ph.D).

5. 10/2/96 Submitted mail protocol revision to VA IRB with amended consent, and received approval of protocol and amended consent.

6. 10/6/96 Submitted first annual report which described revised methodology and the intention to begin mailing within 2 months.

7. 7/9/97 Written approval of first annual report (*reviewed and accepted as written*) received from DA (Pawlus).

8. 7/97 E-mail from PI and Co-PI to Juanita Bourne confirming request to re-budget for mailing (vs. in-person) costs.

9. 9/12/97 Progress note submitted to DA (Friedl) re. updated project status, referring to revised methodology.

10. 2/4/98 Request and approval of contract extension without additional funds for period 3/10/98-9/10/98.

11. 11/17/98 Second progress note submitted to DA (Friedl) re. updated project status, referring to revised methodology.

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Recent Presentations

Erickson, D.J., Huang, M.H., Wolfe, J., Sharkansky, E.J., King, L.A., & King D.W. (1998, November). A Prospective Analysis of Posttraumatic Stress Disorder and Depression Symptoms. Poster session presented at the 14th Annual Meeting if the International Society for Traumatic Stress Studies, Washington DC.

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